



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,087	03/24/2000	Michael J. Detmar	10287-051001	2190

26161 7590 11/20/2003

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
----------	--------------

1642

DATE MAILED: 11/20/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/536,087

Applicant(s)

DETMAR ET AL.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,6,14-18,20-23,53-61,63-67 and 75-122 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6,14-18,20-23,53-61,63-67 and 75-122 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 16.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Applicant's amendment and an **unsigned copy** of Dr. Detmar's declaration filed on 7-30-2003, and IDS filed On 03-10-2003 are acknowledged. Until a signed copy of the declaration arrives, the declaration would not be considered by the Office.

Election/Restrictions

Claims 1, 6, 14-18, 20-23, 53-61, 63-67, and 75-122 are pending and under consideration.

Claim Rejections - 35 USC § 112

Enablement

Claims 1, 6, 14-18, 20-23, 53-61, 63-67, 75-87 **remain rejected** for reason of record and the new claims 88-122 is also rejected under rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 6, 14-18, 20-23, 53-61, 63-67, and 75-121 are drawn to method of treating angiogenesis-dependent cancers by administering a protein with 90 % sequence identity to SEQ ID NO:2 or a fragment thereof capable of inhibiting endothelial migration, wherein said fragment comprises at least 10 contiguous amino acids either a procollagen domain of TSP-2 or a type I repeat of TSP-2 and claim 122 is drawn to method of treating angiogenesis-dependent cancers by administering SEQ ID NO:10.

Applicant argues: the present claims recite specific structures of TSP-2, which have been shown to work in the claimed method and making various fragments or

Art Unit: 1642

mutations in a known protein is a routine molecular biology technique; the data with the TSP-2 nucleic acid transfected tumor cells in nude mice in the specification correlates with in vivo protein therapy; the specification at pages 42-46 has support for protein administration; the first Dr. Detmar's declaration shows in vivo treatment with TSP-2/NTF; the claimed methods simply work and all of the references cited by the Office is irrelevant to claimed invention; the specification gives a plenty of guidance and the level of skill in the art of the claimed invention is very high, therefore the claimed invention is fully enabled.

The arguments have been fully considered but found unpersuasive because the claims are drawn to cancer treatment, not just making a collection of mutants and fragments, which can be done without undue experimentation in the current state of art. As presented in the previous Office action, the cancer treatment art is unpredictable. The Office concurs with applicant's assessment the level of skill in making the fragments and/or making mutants of a known protein sequence using the currently available molecular biology technique is high. However, the instant claims are not drawn to making the fragments and/or making mutants of a known protein sequence per se, but drawn to method of treating cancer by the administration of said mutants or fragments, which is unpredictable for reasons given in the previous Office action; how to use said mutants and fragments for the purpose stated in the preamble of the instant claims requires undue experimentation. Applicant's argument that the specification provides ample examples for how to make the fragments with the recited function is not persuasive either. Although endothelial migration assay is well known in the art, the

Art Unit: 1642

specification does not provide guidance about how to make and use "a fragment thereof capable of inhibiting endothelial cell migration, wherein the fragment comprises **at least 10 contiguous amino acids of either (a) a procollagen domain of TSP-2**" in a method of treating cancer. Compare the bold-faced limitation in the base claim 1 and the data in Fig. 7, which shows Peptide 7 (first type 1 repeat) as the only peptide capable of inhibiting endothelial migration and the rest of peptides comprising at least 10 contiguous amino acids of a procollagen domain of TSP-2 according to page 40 lines 4-7 which do not have the recited function. Applicant's argument using the transfection data in the specification is not commensurate in scope of the claims because instant claims require administering protein or peptide directly. Applicant's argument using the cancer treatment data presented in the first Declaration using about a 600-aa N-terminal specific fragment of TSP-2 is not commensurate in scope of the claims because the claims are **not limited** to method of treating skin cancer or squamous cell carcinoma (A431 cell lines) shown in the declaration using the specific fragment. The specification discusses TSP-2 protein administration broadly at page 42-46 but the specification as originally filed does not teach the specific fragment being used in the first Declaration.

Considering unpredictability in the cancer treatment art, broad scope of claims, insufficient guidance with regard to various recited cancer treatments with various claimed products, it is maintained that undue experimentation would be required to practice the invention as claimed.

Written Description

Claims 1, 6, 14-18, 20-23, 53-61, 63-67, 75, 76, and 84-87 remain rejected for reason of record and claims 88-104, 106-112, 118-121 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 6, 14-18, 20-23, 53-61, 63-67, 75, 76, 84-87, 88-104, 106-112, 118-121 are drawn to method of treating angiogenesis-dependent cancers by administering a protein with 90 % sequence identity to SEQ ID NO:2 or a fragment thereof capable of inhibiting endothelial migration, wherein said fragment comprises at least 10 contiguous amino acids of either a procollagen domain of TSP-2 or a type I repeat of TSP-2.

Applicant argues that the amended claims recite the fragments with specific function and 90 % identity to SEQ ID NO:2, therefore the amended claims meet the Written Description Guidelines. These arguments have been fully considered but found unpersuasive.

The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the claims do not associate any function for 90 % identical structure to SEQ IDNO:2 . Accordingly, in the absence of sufficient recitation of distinguishing identifying functional characteristics, the specification does not provide adequate written

Art Unit: 1642

description of the claimed genus. As for the fragments thereof with the recited function, the specification at Fig. 7 shows Peptide 7 (first type 1 repeat) as the only peptide capable of inhibiting endothelial migration and the rest of the peptides comprising at least 10 contiguous amino acids of a procollagen domain of TSP-2 according to page 40 lines 4-7 which do not have the recited function, thus the recited structures do not match with the recited function. The specification does not teach any structure of a fragment comprising at least 10 contiguous amino acids of a procollagen domain of TSP-2 capable of inhibiting endothelial cells.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of fragments of TSP-2, given Peptide 7 is only species with the recited function. Therefore the full breadth of the claims does not meet the written description provision of 35 U.S.C. §112, first paragraph.

New matter

The rejection of claims 77-79 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is **withdrawn** because applicant's argument is persuasive.

Art Unit: 1642

Claims 1, 6, 14-18, 20-23, 53-61, 63-67, and 75-122 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The base claims 1 and 122 recite "an angiogenesis-dependent tumor". Applicant stated in the amendment that the specification at page 2 lines 15-20, page 18 lines 18-20, pages 28 lines 27-31 and the original claims have support the new amendment. However, although the specification at page 2 line 15-20 has support for unwanted cell proliferation, unwanted angiogenesis, benign or malignant unwanted cell proliferation, it does not have support for the treatment of an angiogenesis-dependent tumor. The specification at page 18 and 28 contemplates the fragments of SEQ ID NO: 2 and the original claims do not support the new limitation "an angiogenesis-dependent tumor", either.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

Art Unit: 1642

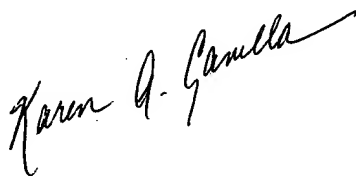
mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
November 14, 2003

A handwritten signature in black ink, appearing to read "Karen A. Gamella", is written over the typed name and date.